

**REMARKS**

Reconsideration and withdrawal of the objections to and rejections of the present application are respectfully requested in view of the remarks herein.

**I. STATUS OF THE CLAIMS AND FORMAL MATTERS**

Claims 1, 4-6, and 8-38 were previously pending, with claims 9, 13, and 26-38 withdrawn from consideration. By this paper claims 4, 10, and 23 are amended, claim 22 is cancelled, and new claims 39 and 40 are added without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents. No new matter is added.

It is submitted that the claims, herewith and as originally presented, are patentably distinct over the prior art cited by the Examiner, and the originally-filed claims and the claims herewith are and were in full compliance with the requirements of 35 U.S.C. §112. The claims amended herein are not amended for purposes of patentability within the meaning of 35 U.S.C. §§§§ 101, 102, 103 or 112. Rather, the amendments to the claims are presented simply for clarification and to round out the scope of protection to which Applicants are entitled. Furthermore, it is explicitly stated that the herewith amendments should not give rise to any estoppel.

**II. THE OBJECTIONS TO THE CLAIMS ARE OVERCOME**

Claim 10 was objected to for being of improper independent form for failing to further limit claim 1, on which it depends. In accordance with the Examiner's suggestion claim 10 has been split into two separate claims. Amended claim 10 is now directed to naturally occurring polyhydroxy compounds, and new claim 39 is directed to synthetic polyhydroxy compounds. Accordingly the objection to claim 10 is overcome.

Claim 11 was objected to for encompassing non-elected species. It is our understanding that upon the allowance of a generic claim, Applicants will be entitled to consideration of claims to additional non-elected species which are written in dependent form or otherwise include all of the limitations of an allowed generic claim as provided by 37 C.F.R. 1.141. Claim 11 depends upon generic claim 1, which Applicants believe to be in condition for allowance. Accordingly, Applicants respectfully request that this objection be held in abeyance pending reconsideration of claim 1 in light of the remarks herein.

In view of the above remarks, reconsideration and withdrawal of the objections to the claims are respectfully requested.

**III. THE REJECTIONS UNDER 35 U.S.C. §112 ARE OVERCOME**

Claims 4-5 and 22-23 were rejected under 35 USC § 112, second paragraph, as being indefinite for allegedly failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Office Action states that the phrase “an amide bond or a peptide bond” in claim 4 and the phrase “binds strongly” in claim 22 are indefinite.

By this paper claim 4 has been amended to delete “a peptide bond” and new claim 40 has been added. Claim 40 depends upon amended claim 4 and is directed to an amide bond that is a peptide bond. In addition claim 22 has been cancelled, and the dependency of claim 23 amended such that it now depends on claim 1 and not cancelled claim 22. Accordingly, reconsideration and withdrawal of the rejections of the claims under 35 USC § 112, second paragraph, are respectfully requested.

**III. THE REJECTIONS UNDER 35 U.S.C. §103(a) ARE OVERCOME**

Claims 1, 4-6, 8, 10-12 and 14-24 were rejected under 35 USC § 103(a), as allegedly being unpatentable over either Cheronis et al. U.S. Patent No. 5,573,916 (“Cheronis”), Chisari et al. U.S. Patent No. 5,709,995 (“Chisari ‘995”), or Chisari et al. U.S. Patent No. 5,780,036 (“Chisari ‘036”) in view of Gregorius et al. Immunological Methods 1995; 181:65-73 (“Gregorius”). The Office Action acknowledges that Cheronis, Chisari ‘995 and Chisari ‘036 fail to teach or suggest coupling of antigenic determinants to a carrier (such as dextran) via nitrogen atoms at their respective N-termini, but asserts that the teaching of Gregorius would have made it obvious to do so. Applicants respectfully traverse these rejections as follows.

Three basic requirements must be met in order to establish a *prima facie* case of obviousness. MPEP §2143. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. MPEP §2143.01, and *In re Laskowski*, 12 U.S.P.Q. 2d 1397, 1399 (Fed. Cir. 1989); *In re Obukowitz*, 27 U.S.P.Q. 2d 1063 (BOPAI 1993). As stated by the Court in *In re Fritch*, 23 U.S.P.Q. 2d 1780, 1783-1784 (Fed. Cir. 1992) “[t]he mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggests the desirability of

the modification.” Second, there must be a reasonable expectation of success. MPEP §2143.02, and In re Merck & Co., Inc., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Finally, the combination of prior references must teach or suggest all of the limitations of the claims. MPEP §2143.03, and In re Royka, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). All words in a claim must be considered in judging the patentability of that claim against the prior art. MPEP §2143.03, and In re Wilson, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970). Applicants respectively assert that none of these three requirements for obviousness are satisfied in the present case, and accordingly the rejection of the claims under 35 U.S.C. §103(a) is not proper.

As regards the third requirement of the obviousness test, the combination of Cheronis, Chisari ‘995 or Chisari ‘036 with Gregorius fails to teach or suggest all of the limitations of the present claims. Gregorius teaches a method for preparing surfaces coated with tresylated dextran. Such surfaces will couple to a biomolecule via a reaction that involves the tresyl group and a nucleophilic group in the biomolecule. However, this coupling reaction is not in any way specific for N-terminal amino groups, as can be seen from Figure 1 of Gregorius. Therefore, a peptide which includes amines other than the amino terminal amine, or which includes a thiol group, will also be able to couple to the tresylated dextran via non-N-terminal amines, unless these non-N-terminal groups are protected. The peptides coupled to tresylated dextran in Gregorius all include non-protected, non-N-terminal nucleophilic groups, because they all include non-protected C(Cys), N (Asn), Q (Gln), K (Lys), R (Arg), H (His), or W (Trp) amino acid residues (see the peptides listed in page 67 of Gregorius in the 1<sup>st</sup> paragraph of the right-hand column). These amino acid residues all include nucleophilic groups that do not form part of the peptide bonds in a polypeptide. Hence, the combination of Cheronis, Chisari ‘995 or Chisari ‘036 with Gregorius fails to teach or suggest immunogens wherein each of the first and second antigenic determinants are coupled to a polyhydroxypolymer carrier through the nitrogen atoms at their N-termini, as recited in the present claims. Rather, the combination of Cheronis, Chisari ‘995 or Chisari with Gregorius would only teach or suggest, if at all, coupling of peptides to a carrier, such as dextran, in a random fashion via any available nucleophilic groups.

The methods of the present invention are able to achieve coupling of each of the first and second antigenic determinants specifically through to nitrogen atoms at their N-termini. This may be achieved, for example, by protecting groups in the antigenic determinants, as described

on page 28 lines 9-17 of the present application. Neither such protection methods, nor such immunogens having each antigenic determinant coupled to a polyhydroxypolymer carrier via the nitrogen atoms at their N-termini, are taught or suggested by the combination of Cheronis, Chisari '995 or Chisari and Gregorius. In summary, because the combination of the cited references fails to teach or suggest all of the limitations of the claims, the third requirement of the test for *prima facie* obviousness has not been met.

As regards the first requirement of the obviousness enquiry, the Examiner asserts that one of skill in the art would be motivated to combine Cheronis, Chisari '995 or Chisari '036 with Gregorius because "direct coupling of the epitopes to the carrier would not require the additional step of modifying the epitope by the addition of a cysteines, thus simplifying the preparation of the epitope being coupled." This reasoning is flawed however, because producing an immunogen wherein each of the first and second antigenic determinants are coupled to a polyhydroxypolymer carrier through nitrogen atoms at their N-termini may require some modification of the epitope, for example protection of certain groups in the epitope before performing the coupling reaction. Thus, prior to the present invention, one of skill in the art would not have been motivated to combine the references as suggested by the Examiner. Thus, the first requirement of the three-prong test for *prima facie* obviousness is also not met.

Finally, as regards the second prong of the test, the Examiner asserts that the expectation of success would be high, since Gregorius teaches that tresyl-activated water-soluble dextran readily binds to peptides which possess nucleophilic groups, such as amino groups. However, the cited art fails to provide any expectation of success in producing immunogens wherein each of the first and second antigenic determinants are coupled to a polyhydroxypolymer carrier through nitrogen atoms at their N-termini. Thus, the second requirements of the three-prong test for *prima facie* obviousness is also not met.

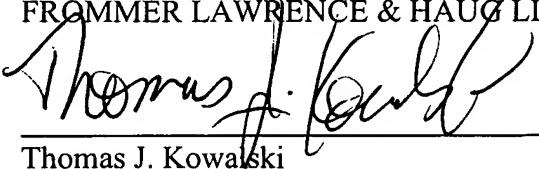
In light of the above remarks, the rejection of the claims as obvious over the combination of Cheronis, Chisari '995 or Chisari '036 and Gregorius has been shown to be improper. Accordingly, reconsideration and withdrawal of the rejections of the claims under 35 USC § 103(a) are respectfully requested.

CONCLUSION

In view of the amendments and remarks herewith, which are fully responsive to the rejections, the application is in condition for allowance. Consideration and entry of this paper, favorable reconsideration of the application and reconsideration and withdrawal of the objections to and rejections of the application, and prompt issuance of a Notice of Allowance are earnestly solicited.

Respectfully submitted,  
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